

REMARKS

Formal Matters

Claims 26, 27, 29, 30 and 32 are pending.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Appeal No. 2004-2319

The Applicants wish to bring to the Examiner's attention and place on the record a decision by the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office.

The decision discusses claims reciting a polypeptide having a "sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO:1".

In the case discussed in the decision, claims reciting a genus of polypeptides were found to *meet* the written description and enablement standards of 35 U.S.C. §112, first paragraph. The claims discussed in the decision were supported by disclosure of a single representative species encompassed by the claims.

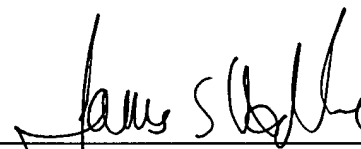
The decision is attached hereto as Exhibit A.

The Examiner is respectfully requested to consider the Board's findings in the attached decision, in replying to the Applicants' response filed on April 25, 2005.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-008CIP.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: May 13, 2005

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EXHIBIT A - 09/715,725

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte OLGA BANDMAN,
NEIL C. CORLEY, and PURVI SHAH

Appeal No. 2004-2319
Application No. 09/915,694

ON BRIEF

Before WILLIAM F. SMITH, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 3, 6, 7, 9 and 12. Claims 3 and 12 are representative of the subject matter on appeal, and read as follows:

3. An isolated polynucleotide encoding a polypeptide selected from the group consisting of:
 - a) a polypeptide comprising the amino acid sequence of SEQ ID NO: 1; and
 - b) a polypeptide comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1.

12. An isolated polynucleotide selected from the group consisting of:
 - a) a polynucleotide comprising the polynucleotide sequence of SEQ ID NO: 2,
 - b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2,
 - c) a polynucleotide having a sequence complementary to a polynucleotide of a),
 - d) a polynucleotide having a sequence complementary to a polynucleotide of b) and
 - e) an RNA equivalent of a)-d).

The examiner relies upon the following references:

Attwood et al. (Attwood), "Which craft is best in bioinformatics?," Computer and Chemistry, Vol. 25, pp. 329-339 (2001)

Ponting, "Issue in predicting protein function from sequence," Briefing in Bioinformatics, Vol. 2, No.1, pp. 19-29 (2001)

Claims 3, 6, 7, 9 and 12 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In addition, the claims stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. After careful review of the record and consideration of the issues before us, we reverse both rejections. We do, however, enter a new ground of rejection under 35 U.S.C. § 112, second paragraph over claim 12.

DISCUSSION

Written Description

Claims 3, 6, 7, 9 and 12 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventors, at the time the application was filed, had possession of the claimed invention.

According to the rejection:

The claimed invention encompass[es] [sic] any isolated polynucleotide encoding any polypeptide comprising any naturally occurring amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1 (claim 3) and any isolated polynucleotide comprising any naturally occurring polynucleotide sequence that is at least 95% identical to the nucleotide sequence of SEQ ID NO: 2 (claim 12).

Examiner's Answer, page 3.

The rejection contends that the specification provides only a single representative species—an isolated polynucleotide consisting of SEQ ID NO: 2. The rejection asserts that “[t]here is no disclosure of any particular structure to function/activity relationship in the single disclosed species.” *Id.* The rejection concludes “[g]iven this lack of additional representative species as encompassed by the claims, [appellants] have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize [appellants] were in possession of the claimed invention.

The written description requirement of 35 U.S.C. § 112, first paragraph, does not require a description of the complete structure of every species within a chemical genus. *See Utter v. Hiraga*, 845 F.2d 993, 998, 6 USPQ2 1709, 1714 (Fed. Cir. 1988) (“A specification may, within the meaning of 35 U.S.C. § 112, ¶ 1, contain a written description of a broadly claimed invention without describing all species the claim encompasses.”).

The Court of Appeals for the Federal Circuit, our reviewing court, has addressed the issue of what constitutes adequate written description for a claim drawn to a nucleic acid. In Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1602 (Fed. Cir. 2002), the court adopted a portion of the Guidelines proffered by the United States Patent and Trademark Office (USPTO). The court stated that:

The written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.

Enzo Biochem, 296 F.3d at 1324, 63 USPQ2d at 1613 (citations omitted).

In Enzo-Biochem, the court refined the approach advanced by The Regents of The University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1998), adopting an example offered in the USPTO guidelines having facts that contrasted with those of Eli Lilly, wherein the written description requirement would be met. Adequate written description may be present for a genus of nucleic acids based on their hybridization properties, "if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar." Enzo Biochem, 296 F.3d at 1327, 63 USPQ2d at 1615.

In the case before us, the complete structure of the polynucleotide of SEQ ID NO: 2 has been described, and the genus limited to a polynucleotide comprising a naturally occurring polynucleotide sequence at least 95% identical

to the polynucleotide sequence of SEQ ID NO: 2. In addition, the complete structure of the polypeptide of SEQ ID NO: 1 has been described, and the genus limited to polypeptides comprising a naturally occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1. While the examiner asserts that the specification provides no disclosure of any particular structure to function/activity relationship in the single disclosed species, the examiner has not adequately explained and/or provided evidence to support that assertion. Thus, the rejection of claims 3, 6, 7, 9 and 12 under 35 U.S.C. § 112, first paragraph, for lack of adequate written description, is reversed.

Enablement

Claims 3, 6, 7, 9 and 12 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

According to the rejection:

The claimed invention encompass[es] [sic] any isolated polynucleotide encoding any polypeptide comprising any naturally occurring amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1 (claim 3) and any isolated polynucleotide comprising any naturally occurring polynucleotide sequence that is at least 95% identical to the nucleotide sequence of SEQ ID NO: 2 (claim 12).

Examiner's Answer, page 4.

The rejection contends that while the specification provides guidance for an isolated polynucleotide consisting of SEQ ID NO: 2, it "does not teach the

specific structural /catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered.” Id. The rejection asserts further that

The amount of experimentation to make the claimed polynucleotide is enormous and undue and entails selecting specific nucleotides to change (deletion insertion, substitution, or combinations thereof) in any polynucleotide to make a polynucleotide encoding a polypeptide comprising an amino acid sequence that is at least 95% identical to SEQ ID NO: 1 or selecting specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in the nucleotide sequence of SEQ ID NO: 2 to make a polynucleotide that has a nucleotide sequence that is at least 95% identical to SEQ ID NO: 2 and determining by assays whether the encoded polypeptide has malate dehydrogenase activity.

Id. at 5.

Appellants argue that “[i]ndependent claim 3 recites not only that the ‘variant’ polynucleotides encode polypeptides that are at least 95% identical to SEQ ID NO: 1, but also have ‘a naturally occurring amino acid sequence.’” Appeal Brief, page 10 (emphasis in original). Thus, appellants contend, “through the process of natural selection, nature will have determined the appropriate amino acid sequences,” and given the information provided by SEQ ID NO: 1, the specification enables one skilled in the art to obtain a polynucleotide encoding a polypeptide comprising a naturally-occurring amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1. We agree.

The examiner bears the initial burden of showing nonenablement. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). “[E]nablement requires that the specification teach those in the art to make and use the invention without ‘undue experimentation.’ . . . That some

experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (emphasis in original). Some experimentation, even a considerable amount, is not "undue" if, e.g., it is merely routine, or if the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The examiner argues that "[t]he recitation of 'naturally occurring amino acid sequence' in the claims does not meet the enablement requirement since the specification must still provide guidance regarding the specific amino acid residues in the amino acid sequence of SEQ ID NO: 1 which cannot be changed and amino acid residues which can be changed but still retain malate dehydrogenase." Examiner's Answer, page 14. That argument is not agreed with because the examiner has not explained and/or provided evidence why a naturally occurring polynucleotide sequence that is at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2, or a naturally occurring polypeptide that is at least 95% identical to the amino acid sequence of SEQ ID NO: 1 would not have malate dehydrogenase activity. As explained by appellants, "through the process of natural selection, nature will have determined the appropriate amino acid sequences." Thus, the rejection of claims 3, 6, 7, 9 and 12 under 35 U.S.C. § 112, first paragraph, for lack of enablement, is reversed.

NEW GROUND OF REJECTION

Under the provisions of 37 CFR § 41.50(b), we enter the following new ground of rejection: Claim 12 is rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The scope of the claim is indefinite because of its recitation of "a naturally occurring polynucleotide sequence at least 95% identical to the polynucleotide sequence of SEQ ID NO: 2 . . . [and] an RNA equivalent [thereof]."

The normal meaning of "polynucleotide" is a polymer made up of nucleotides. Nucleotides are made up of a purine or pyrimidine base joined to a sugar residue (deoxyribose in DNA, ribose in RNA) and a phosphate group. Thus, according to its normal meaning, part (b) of claim 12 would encompass both DNA and RNA. Read in light of the rest of the claim and the specification, however, the scope of the claim becomes unclear.

First, SEQ ID NO:2 is a DNA sequence since it contains thymine (T) residues. The equivalent RNA sequence would have uracil (U) in place of thymidine. It is unclear, however, whether T and U would be considered to be "identical" residues in computing whether a given polynucleotide was "95% identical" to SEQ ID NO:2.

Second, if part (b) of claim 12 is intended to include both DNA and RNA, then part (e) of the claim is entirely superfluous. That is, there would be no need for a part (e) directed to "RNA equivalent[s]" unless parts (a) through (d) of claim 12 are intended to be limited to DNA, rather than encompassing both DNA and RNA.

These factors suggest that claim 12 uses the term "polynucleotide" as a synonym for DNA, rather than using it in its usual sense of encompassing both DNA and RNA. However, construing part (b) of the claim as limited to DNA presents its own problems. If part (b) of claim 12 were construed to encompass only "naturally occurring [DNA] sequence[s] at least 95% identical to the [DNA] sequence of SEQ ID NO:2", that part of the claim would very likely define a compound that does not exist.

The DNA shown in the specification's SEQ ID NO:2 is a cDNA sequence. See, working examples I, II and III (headed "THP1PLB01 cDNA Library Construction," "Isolation and Sequencing of cDNA Clones," and "Homology Searching of cDNA clones and Their Deduced Proteins," respectively).

cDNA sequences are not naturally occurring. They are laboratory-made DNA copies of naturally occurring messenger RNA (mRNA) sequences. The only naturally occurring DNA sequence that encodes the protein of SEQ ID NO:1 is a genomic sequence. That genomic sequence is then transcribed by the cell into an RNA equivalent that is processed and eventually translated into the polypeptide of SEQ ID NO:1. The processing steps required to generate an mRNA from a genomic DNA include removal of intervening sequences, or introns.

Virtually all human genes include introns. Thus, those skilled in the art would expect that the naturally occurring gene encoding the polypeptide of SEQ ID NO:1 would be interrupted by several introns. As a result, those skilled in the art would expect that, more likely than not, no naturally occurring DNA would be

95% identical to SEQ ID NO:2 because the parts of the naturally occurring gene that are identical to SEQ ID NO:2 would be interrupted by introns that are not part of the cDNA sequence of SEQ ID NO:2.

The naturally occurring gene that encodes the polypeptide of SEQ ID NO:1 would only fall within the scope of part (b) of claim 12 if it has introns that comprise 5% or less of its sequence. If the naturally occurring gene contains greater than 5% introns, it would appear that there is no naturally occurring DNA sequence that is 95% identical to SEQ ID NO:2. Thus, if part (b) of claim 12 is construed as being limited to DNA, it is overwhelmingly likely to be a nullity. It would add nothing to the scope of the claim.

On the other hand, if part (b) of claim 12 were construed to encompass both DNA and RNA, in addition to the ambiguities discussed above it would present issues of enablement that have not been discussed on the record. That is, if the claim encompasses both DNA and RNA, and if the corresponding genomic DNA does not contain an anomalously small amount of intron DNA, the only "naturally occurring" polynucleotides that would be 95% identical to SEQ ID NO:2 would be mRNAs (which are processed to excise introns).

Claim 12 is directed to an "isolated" polynucleotide, but the specification provides no guidance on how to isolate the particular mRNA corresponding to SEQ ID NO:2. Thus, if part (b) of claim 12 is construed to encompass both DNA and RNA, then for the reasons discussed above, the DNA aspect is probably a nullity and it is unclear whether the specification provides adequate guidance to

enable those skilled in the art to make and use the mRNA that represents the remainder of the invention defined by part (b).

Finally, even assuming that part (b) of claim 12 were construed to encompass naturally occurring mRNAs that are at least 95% identical to SEQ ID NO:2, and assuming that the specification provides an enabling disclosure for such mRNAs, the scope of the claims would still be unclear. The specification provides no guidance that would allow those skilled in the art to determine, with a reasonable degree of confidence, whether any of the sequences that are at least 95% identical to SEQ ID NO:2 occur naturally and, if so, which they would be. The only way to definitely fix the scope of the claims would be to compare SEQ ID NO:2 to all naturally occurring sequences, clearly an impossible task. Thus, even if we were to ignore the various ambiguities discussed above, the metes and bounds of the claim are unclear.

As the Federal Circuit recently noted,

[t]he Supreme Court explained the reason underlying the indefiniteness doctrine 60 years ago in United Carbon Co. v. Binney & Smith Co., 317 U.S. 228, 236, 55 USPQ 381, 385 (1942):

A zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims would discourage invention only a little less than unequivocal foreclosure of the field. Moreover, the claims must be reasonably clear-cut to enable courts to determine whether novelty and invention are genuine.

Exxon Research and Eng'g Co. v. United States, 265 F.3d 1371, 1376, 60

USPQ2d 1272, 1276 (Fed. Cir. 2001). The court held that compliance with 35

U.S.C. § 112, second paragraph, is determined by “whether ‘the claims at issue

[are] sufficiently precise to permit a potential competitor to determine whether or

not he is infringing.” Id. (bracketed text in original, quoting Morton Int’l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993)). That test is not met here.

For all these reasons, the scope of claim 12 is unclear. The test for definiteness is “whether one skilled in the art would understand the bounds of the claim when read in light of the specification.” Miles Laboratories Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). See also Amgen, Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1342, 65 USPQ2d 1385, 1406 (Fed. Cir. 2003): “[A]mbiguity in claim scope is at the heart of the definiteness requirement of 35 U.S.C. § 112, ¶ 2.” Since we cannot determine the scope of claim 12, we conclude that it is indefinite. Claim 12 is rejected under 35 U.S.C. § 112, second paragraph.

TIME PERIOD FOR RESPONSE

This decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides “[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review.”

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

(1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .

(2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .



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No time period for taking any subsequent action in connection with this
appeal may be extended under 37 CFR § 1.136(a).

REVERSED, 37 CFR § 41.50(b)

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